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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/524,134	02/11/2005	Scott Koenig	11183-003-999	1503

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EXAMINER	
CROWDER, CHUN	
ART UNIT	PAPER NUMBER
1644	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	12/29/2006	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/524,134	KOENIG ET AL.	
	Examiner	Art Unit	
	Chun Crowder	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10/10/2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-109* is/are pending in the application.

4a) Of the above claim(s) *2-8,22,24-29,33-37,39,40,44-80 and 91-103* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,9-21,23,30-32,38, 41-43, 81-90 and 104-109* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/10/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendments, filed 10/10/2006, are acknowledged.

Claims 1, 9, 81-90 have been amended.

Claims 1-109 are pending.

Claims 2-8, 22, 24-29, 33-37, 39, 40, 44-80, 91-103 have been withdrawn from further consideration, as being drawn to nonelected inventions.

Claims 1, 9-21, 23, 30-32, 38, 41-43, 81-90, 104-109 are currently under consideration as they read on originally elected invention of an isolated antibody of clone 2B6 without conjugation that binds to native FcγRIIB with greater affinity than FcγRIIA and antagonizes at least one activity of FcγRIIB.

2. The instant application appears to be in sequence compliance for patent applications containing nucleotide sequence and/or amino acid sequence disclosures.

3. This Office Action will be in response to applicant's arguments, filed 10/10/2006.

The rejections of record can be found in the previous Office Action, mailed 04/10/2006.

The text of those Sections of Title 35 U.S.C. not included in this Action can be found in a prior Action.

4. Applicant's IDS, filed 10/10/2006, is acknowledged and has been considered.

5. Applicant's amendments to the specification filed 10/10/2006 are acknowledged and have been entered.

6. Upon further consideration as well as applicant's amendment, the previous rejections under **35 U.S.C. 112, second paragraph** against claims 9, 12, 41, and 109 have been withdrawn.

7. Upon further consideration as well as applicant's submission of the Statement Regarding the Permanence and Availability of Deposited Microorganisms under 37 C.F.R. 1.1801-1.809, filed 10/10/2006, the conditions for the deposit of biological material under 35 USC 112, first paragraph with respect to hybridoma 2B6 having ATCC accession number PTA-4591 appear to have been satisfied; thus the previous rejection under **35 U.S.C. 112, first paragraph** against claims 38 and 41-43 has been withdrawn.

8. Claims 12, 31, 41, and 109 are rejected under **35 U.S.C. 112, second paragraph**, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for reasons of record.

A) Claim 12 is indefinite in the recitation of "B cell activity" because the metes and bounds of the "B cell activity" is not clear and ambiguous.

As applicant indicated in the Remark, filed 10/10/2006, that claim 14 does not recite "B cell activity"; therefore claim 14 is not included herein. The examiner apologized for any inconvenience in this matter.

Applicant's argument has been fully considered but has not been found persuasive.

Applicant argues that the term "B cell activity" is well understood in the art, as such one of skill in the art could readily ascertain the meaning of the term.

This is not found convincing for following reasons of record. In addition, it is not clear it is unclear as to which "B cell activity" or the requisite structural/functional characteristic is/are intended or encompassed by the claimed antibody.

Applicant is once again suggested to amend the claims to recite the "B cell activity" encompassed by the claimed antibody. See claim 13 for example.

B) Claim 31 is indefinite in the recitation of "immune response" because the metes and bounds of the "immune response" is not clear and ambiguous.

Applicant's argues that the FcγRIIB receptor is associated with inhibitory signaling in immune cells; thus the claimed antibody would block the inhibitory signal.

This is not found persuasive for reasons of record. Further, it is unclear as to which "immune response" or the requisite structural/functional characteristic is/are intended or encompassed by the claimed antibody.

Applicant is once again suggested to amend the claims to recite the "immune response " encompassed by the claimed antibody. See claim 32 for example.

9. Claims 1, 9-16, 23, 30-32, 81-90, 108, and 109 are rejected under **35 U.S.C. 102(b)** as being anticipated by Weinrich et al. (Hybridoma. 1996, 15;2:109-116. Reference C68 in IDS) as evidenced by Bolland et al. (Advances in Immunology. 1999. 72:149-177. Reference C04 in IDS) and Clynes et al. (Nature Medicine. 2000. 6;4:443-446. Reference C15 in IDS) for reasons of record.

Applicant's arguments in conjunction with the Koenig declaration under 37 C.F.R. 1.132 have been fully considered but have not been found persuasive.

It is noted that claims 1, 9-16, 23, 30-32, 81-90, 108, and 109 are rejected under **35 U.S.C. 102(b),** not under 35 U.S.C. 102(a) as indicated on page 18 of the Remark filed 1010/2006.

Applicant argues that the instant claims have been amended to add the limitation of "wherein said variable domain specifically binds FcγRIIB that is endogenously expressed on the surface of a cell"; thus the prior art monoclonal antibody II8D2 taught by Weinrich et al. would not anticipate the instant claims because according to Budde et al (Leukocyte Typing V: White Cell differentiation antigens. 1995;828-832. Reference C09 on IDS), the monoclonal antibody II8D2 only reactive with recombinantly expressed FcγRIIB in BHK-21 cells and do not bind FcγRIIB expressed endogenously expressed on Daudi cells (see page 828).

Applicant further asserts that another antibody, KB61, taught by Budde et al. that shows greater reactivity with IIA1.6 cells that recombinantly express FcγRIIbl or FcγRIIb2 than with IIA1.6 cells that recombinantly express FcγRIIaLR or FcγRIIaHR (see Budde, Table I, page 829). However, applicants argues that Budde et al. provides no controls for this experiment (such as normalizing based on the level of expression of the recombinant protein and/or demonstrating a lack of binding in non-transfected cells), or any discussion thereof, providing no basis for comparison of the antibody's reactivity among independently transfected cell lines. In addition, Budde reports that KB61 exhibits similar reactivity to FcγRIIa and FcγRIIb expressed in BHK-21 cells, Daudi, and K-562 cells. Applicant further asserts that experiments conducted to investigate the binding specificity of KB61 using surface plasmon resonance demonstrate that KB61 exhibits similar binding to FcγRIIB and FcγRIIA within statistical error (see Exhibit *C*, Declaration of Dr. Scott Koenig, in particular paragraphs 5 and 6, and Exhibit 5).

Accordingly, applicant argues that Budde et al. does not disclose an antibody or fragment thereof comprising a variable domain that specifically binds to FcγRIIB with greater affinity than to FcγRIIA. Thus, like Weinrich, Budde et al. do not anticipate the claimed invention.

This is not found persuasive for following reasons:

Contrary to applicant's assertion that "FcγRIIB that is endogenously expressed on the surface of a cell" excludes recombinantly expressed FcγRIIB, it is noted that during patent examination, the pending claims must be "given their broadest reasonable interpretation consistent with the specification". See MPEP 2111.

This means that the words of the claim must be given their plain meaning unless the plain meaning is inconsistent with the specification. In re Zletz, 893 F.2d 319, 321, 13 USPQ2d 1320, 1322 (Fed. Cir. 1989).

Here, the plain meaning of "endogenous" is "produced or synthesized within the organism" (see Merriam-Webster's Collegiate Dictionary 1997 10th Edition, page382, left column); as such "FcγRIIB that is endogenously expressed on the surface of a cell" would include the recombinantly expressed FcγRIIB on the surface of cells.

Further, the instant specification discloses working examples of testing the claimed antibody on staining CHO cells recombinantly expressing FcγRIIB and concludes the claimed antibody binds FcγRIIB (e.g. see pages 130-137 of the instant specification).

Furthermore, in the Koenig declaration under 37 C.F.R. 1.132, filed 10/10/2006, tested binding of monoclonal antibodies KB61 to FcγRIIA or FcγRIIB extracellular domains recombinantly expressed in 293H.

Therefore, in the absence of an express intent to impart a novel meaning to the claimed "FcγRIIB that is endogenously expressed on the surface of a cell", the phrase is presumed to take on the ordinary and customary meanings attributed to them by those of ordinary skill in the art; as such "FcγRIIB that is endogenously expressed on the surface of a cell" would read on the recombinantly expressed FcγRIIB cells.

Therefore, the antibody taught by Weinrich et al. would anticipate the claimed invention.

The rejections of record are maintained for the reasons of record, as they apply to the amended claims. The rejections of record are incorporated by reference herein as if reiterated in full.

10. Claims 1 and 17-21 are rejected under **35 U.S.C. 103(a)** as being unpatentable over Reff et al. (Critical Review in Oncology/Hematology. 2001. 40:25-35) in view of Ott et al. (J. Allergy Clin. Immunol. 2001. 108:S95-S98) and Weinrich et al. (Hybridoma. 1996, 15;2:109-116. Reference C68 in IDS) for reasons of record.

Applicant's arguments in conjunction with the Koenig declaration under 37 C.F.R. 1.132 have been fully considered but have not been found persuasive.

Applicant's arguments and the examiner's rebuttal regarding the teachings of Weinrich et al. have been discussed, supra.

Further, applicant argues that Reff et al. do not teach or suggest the claimed antibody; although Ott et al. recognizes that FcγRIIB may be therapeutic targets in the treatment of immunologic disorders, Ott et al. do not teach effective targeting FcγRIIB. Furthermore, applicant introduces the teachings of Tam et al. (Allergy 2004, 59:772-780. Reference C58 on IDS filed 07/15/2005) and asserts that Tam et al. express skepticism that antibody specific for the extracellular domain of FcγRIIB with greater affinity than that of FcγRIIA can be developed.

This is not found convincing for following reasons:

In response to applicant's arguments against the references individually, one cannot show non-obviousness by attacking references individually where the rejections are based on combination of references. See MPEP 2145.

It is noted that in considering the disclosure of a reference, it is proper to take into account not only specific teaching of the reference but also the inferences which one skilled in the art would be reasonably be expected to draw therefrom In re Preda, 401 F.2d 825, 159 USPQ 342, 344 (CCPA 1968). See MPEP 2144.01.

Furthermore, specific statements in the references themselves which would spell out the claimed invention are not necessary to show obviousness, since questions of obviousness involves not only what references expressly teach, but what they would collectively suggest to one of ordinary skill in the art. See CTS Corp. v. Electro Materials Corp. of America 202 USPQ 22 (DC SNY); and In re Burckel 201 USPQ 67 (CCPA). In re Burckel is cited in MPEP 716.02.

Here, given the teachings of Reff et al. regarding the advantages of humanized or human antibody, single chain antibody and antibody fragments, and the teachings of Ott et al. and Weinrich et al. regarding FcγRIIB being a potential therapeutic target and the method of making anti- FcγRIIB specific antibody, the ordinary artisan at the time the invention was made would have had a reasonable expectation of success of producing humanized or human anti-FcγRIIB specific antibody, single chain or antibody fragments that are specific for FcγRIIB.

The Exhibit D under 37 CFR 1.132, filed 10/10/2006, is insufficient to overcome the rejection of claim1 and 17-21 based upon 35 U.S.C. 103(a) as set forth in the last Office action because: antibody specific for the extracellular domain of FcγRIIB with greater affinity than that of FcγRIIA have been developed as discussed above in Section 9.

Further, applicant argues that the problem of producing an antibody specific for the extracellular domain of FcγRIIB with greater affinity than that of FcγRIIA has long been recognized in the art. However, there is no showing that others of ordinary skill in the art were working on the problem and if so, for how long. In addition, there is no evidence that if persons skilled in the art who were presumably working on the problem knew of the teachings of the above cited references, they would still be unable to solve the problem. See MPEP § 716.04.

In view of the foregoing, when all of the evidence is considered, the totality of the rebuttal evidence of nonobviousness fails to outweigh the evidence of obviousness.

Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

The rejections of record are maintained for the reasons of record, as they apply to the amended claims. The rejections of record are incorporated by reference herein as if reiterated in full.

11. Claims 1 and 104-107 are rejected under 35 U.S.C. 103(a) as being unpatentable over Presta (US Patent 6,737,056) in view of Ott et al. (J. Allergy Clin. Immunol. 2001. 108:S95-S98) and Weinrich et al. (Hybridoma. 1996, 15;2:109-116. Reference C68 in IDS) for reasons of record.

Applicant's arguments have been fully considered but have not been found persuasive.

Applicant's arguments and the examiner's rebuttal regarding the teachings of Ott et al. and Weinrich et al. have been discussed, supra in Sections 7-10.

Further, applicant argues that Presta teach the modification of the Fc region of antibodies to alter binding to an FcγR: Presta does not teach an antibody specific for the extracellular domain of FcγRIIB with greater affinity than that of FcγRIIA.

This is not found persuasive for following reasons:

In response to applicant's arguments against the references individually, one cannot show non-obviousness by attacking references individually where the rejections are based on combination of references. See MPEP 2145.

It is noted that in considering the disclosure of a reference, it is proper to take into account not only specific teaching of the reference but also the inferences which one skilled in the art would be reasonably be expected to draw therefrom In re Preda, 401 F.2d 825, 159 USPQ 342, 344 (CCPA 1968). See MPEP 2144.01.

Furthermore, specific statements in the references themselves which would spell out the claimed invention are not necessary to show obviousness, since questions of obviousness involves not only what references expressly teach, but what they would collectively suggest to one of ordinary skill in the art. See CTS Corp. v. Electro Materials Corp. of America 202 USPQ 22 (DC SNY); and In re Burckel 201 USPQ 67 (CCPA). In re Burckel is cited in MPEP 716.02.

Here, given the teachings of Presta regarding modifying Fc region of antibodies to achieve enhanced ADCC, and the teachings of Ott et al. and Weinrich et al. regarding FcγRIIB being a potential therapeutic target and the method of making anti- FcγRIIB specific antibody, the ordinary artisan at the time the invention was made would have had a reasonable expectation of success of producing Fc modified anti-FcγRIIB specific antibody with increased affinity for FcγRIII and enhanced ADCC.

Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

The rejections of record are maintained for the reasons of record, as they apply to the amended claims. The rejections of record are incorporated by reference herein as if reiterated in full.

12. Claims 1, 9-21, 23, 30-32, 38, 41-43, 81-90, 104-109 are provisionally rejected on the ground of **nonstatutory obviousness-type double patenting** as being unpatentable over claims 1-13 and 16-20 of copending USSN. 11/305,787.

Applicant requests that the provisionally rejection be held in abeyance until allowable subject matter has been identified in the instant application and USSN 11/305,787.

Given that no terminal disclaimer signed by the assignee and fully complied with 37 CFR 3.73(b) was filed, the provisional rejection on the ground of nonstatutory obviousness-type double patenting is maintained.

Applicant is once again reminded that a timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

13. It is noted that applicant acknowledged on page 22 of the Remarks, filed 10/10/2006, that the copending USSN 11/605,787 and the instant application were commonly owned by MacroGenics Inc at the time the invention was made.

14. The hybridoma clone 2B6 does not appear to be taught by the prior art.

15. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chun Crowder whose telephone number is (571) 272-8142. The examiner can normally be reached Monday through Friday from 8:30 am to 5:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Chun Crowder, Ph.D.
Patent Examiner
December 14, 2006

PHILLIP GAMBEL, PH.D
PRIMARY EXAMINER
1600
12/20/2006